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EXAMINER	
QUAN, ELIZABETH S	
ART UNIT	**PAPER NUMBER**
1743	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	**Application No.** 09/619,416	**Applicant(s)** ERDEN ET AL.	
	Examiner Elizabeth Quan	**Art Unit** 1743	

-- Th MAILING DATE of this communication app ars on th cover she t with th correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-53* is/are pending in the application.

4a) Of the above claim(s) *38-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-37 and 42-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 2, 10, 17-19, 21-25, 29, 31, 33-35, 37, 42-47, 49, and 51-53 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,324,483 to Cody et al.

Referring to claims 1, 10, 17-19, 21-25, 29, 31, 33-35, 37, 42-47, 49, and 51-53, Cody et al. disclose an apparatus for multiple, simultaneous synthesis of compounds (10) (see ABSTRACT; FIGS. 2, 4, and 5; COL. 7, lines 37-39). A base (15) with a plurality of reaction wells (16) formed in the upper surface of the base and extending partially therethrough (see FIGS. 2, 4, and 5; COL. 8, lines 23-26). Each of the reaction wells (16) has a closed lower end defined by the base (15) and an open upper end for receiving components for the reaction (see FIGS. 2, 4, and 5). A plurality of vials (11) is inserted into the wells (16) for receiving reaction components (see FIGS. 2, 4, and 5; COL. 8, lines 38-45). A cover (20) is configured for sealing engagement with the base (15) to form a housing enclosing the reaction wells (16) and defining a common pressure chamber in communication with the reaction wells (16) (see FIGS. 2, 4, and 5; COL. 9, lines 16-36; COL. 10, lines 33-37). The cover is removably attached to the base member with quick operating fastening devices (35,36) (see COL. 10, lines 13-37).

A flow restriction device (26) is positioned adjacent to the open ends of the reaction wells (16) aligning the vent holes with the wells to provide communication between the wells and pressure chamber while reducing cross-talk between the wells (see FIGS. 2, 4, and 5; COL. 9, lines 42-61). The flow restriction device (26) is removably attached to the base (15) with fastening means (35,36) (see FIGS. 2, 4, and 5; COL. 10, lines 13-37). The flow restriction device (26) may be a rigid elastomeric, solvent-resistant sheet from rubbers, such as neoprene, silicone, or VITON (see COL. 9, lines 58-61). The sheet has holes, lending it porous (see FIGS. 2, 4, and 5).

An inlet port (23) is in communication with the pressure chamber for supplying pressurized fluid to the chamber to pressurize the reaction wells (16) (see FIGS. 2, 4, and 5; COL. 9, lines 27-34). The housing is made of materials (metals) capable of sustaining a pressure substantially above atmospheric pressure as required for organic synthesis (see COL. 8, lines 29-38; COL. 9, lines 25-27 and 34-36).

Therefore, Cody et al. include all the limitations in claims 1, 10, 17-19, 21-25, 29, 31, 33-35, 37, 42-47, 49, and 51-53.

Claim Rejections - 35 USC § 103

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 2-4, 52, and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,324,483 to Cody et al. as applied to claim 1 above, and further in view of U.S. Patent No. 5,428,118 to Painter et al., "Investigation of Coolant Mixing in Pressurized Water

Reactors at the Rossendorf Mixing Test Facility Rocom" to Grunwald et al., and "Runaway in Stirred Tanks" to Heiszwolf.

Referring to claims 2-4, 52, and 53, while Cody et al. do not quantify internal pressures within the reactor, they disclose a housing from transparent material such as plexiglass. Painter et al. disclose a plexiglas reactor configured to withstand 10 psi to about 1000 psi (see COL. 5, lines 24-26; COL. 7, lines 40-68). Painter et al. address the issue of carrying out operations requiring elevated pressures and/or handling reactive materials at elevated pressures. However, Painter et al. do not explicitly disclose the use of transparent plexiglass; however, it is well known to use a transparent plexiglass to allow observation of reactions as evidenced by Grunwald et al. and Heiszwolf. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to make the synthesis apparatus disclosed by Cody et al. to allow operating pressures as high as 1000 psig as necessary for particular operations and reactants in view of Painter et al. and permit visual observation of reactions as evidenced in Grunwald et al. and Heiszwolf.

5. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,324,483 to Cody et al. as applied to claim 1 above, and further in view of U.S. Patent No. 3,617,033 to Ichikawa et al.

Referring to claim 5, Cody et al. do not specifically state titanium as a material for reactor construction. Ichikawa et al. disclose an experiment using a titanium pressure vessel (see COL. 8, lines 6). While Ichikawa et al. do not explicitly state why the pressure vessel is made from titanium, it appears titanium can withstand high pressures

and is corrosion resistant. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to make the synthesis apparatus disclosed by Cody et al. from titanium for the advantages of withstanding high pressures and corrosion resistance in the event the internal reactor vessels rupture.

6. Claims 6, 7, 9, 11, 12, 16, 26, 27, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,324,483 to Cody et al. as applied to claims 1, 17, 25, 42, and 49 above, and further in view of U.S. Patent No. 6,309,608 to Zhou et al.

Referring to claims 6 and 7, Cody et al. do not disclose using stainless steel and aluminum alloys for the cover of the apparatus. Zhou et al. disclose constructing the reaction block from stainless steel and aluminum alloys, which are readily machined and exhibits high thermal conductivity (see COL. 11, lines 36-46). Zhou et al. do not address the cover; however, it would have been obvious to one having ordinary skill in the art at the time the invention was made to make both the cover and base disclosed by Cody et al. from a single material selected from stainless steel or aluminum alloys for the advantages of ease in machining and high thermal conductivity.

Referring to claim 9, Cody et al. do not disclose a pressure relief valve coupled to an outlet port in communication with the pressure chamber. Zhou et al. disclose venting the reaction block through a pressure relief valve (see COL. 21, lines 37-40). Furthermore, pressure-control means are provided in the purge gas exit line to control the pressure within the reaction block to avoid pressure buildup and safety hazards (see COL. 21, lines 41-44). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include a pressure relief valve to an outlet port in

communication with the pressure chamber as in Zhou et al. to the apparatus of Cody et al. to avoid pressure buildup and the associated hazards.

Referring to claim 11, Cody et al. do not explicitly disclose external dimensions of the base and cover corresponding to standard microtiter plate dimensions. Zhou et al. disclose semi-automated or automated resin washing and reactant dispensing to selected reaction vessels within a standard microtiter plate with a footprint of 3-3/8" by 5" to enhance productivity of all phases of combinatorial synthesis (see COL. 10, lines 19-21; COL. 26, lines 20-56; COL. 27, lines 1-7). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to standardize the dimensions of the synthesis apparatus to allow automation to enhance productivity.

Referring to claim 12, Cody et al. do not explicitly disclose 96 reaction wells arranged in an 8 by 12 array. Zhou et al. disclose transferring synthesized compounds in the first and second of a pair of 48-vessel reaction blocks to odd-numbered and even-numbered wells, respectively, to fill 96 wells (see COL. 58-64; FIG. 17A and 17B). Furthermore, it is well known in the art to use plates with 96 wells in a 12 by 8 array. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use a plate with 96 wells in a 12 by 8 array to conform to convention to allow automation.

Referring to claim 16, Cody et al. do not address the spacing of the reaction wells. Zhou et al. disclose center-to-center spacing of wells in a standard 96-well plate to be about 9 mm (see COL. 28, lines 63-67; COL. 29, lines 1-3). Additionally, it is well known in the art to have 9 mm center-to-center spacing in a 96-well plate. Therefore, it

would have been obvious to one having ordinary skill in the art at the time the invention was made to use 9 mm center-to-center spacing among wells to conform standards and allow automation configured to such standards.

Referring to claim 26, Cody et al. do not disclose springs at the bottom of the reaction wells for biasing the vials upward against the flow restriction device (see FIGS. 2, 4, and 5). Zhou et al. disclose a plurality of springs (490) disposed at the bottom of the reaction wells for biasing the vials upward against the flow restriction device to relieve excessive reaction vessel pressures while maintaining an effective seal between the flow restriction device and vials (see FIGS. 1 and 5A-F; COL. 16, lines 17-19; COL. 21, lines 58-67). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the apparatus of Cody et al. to include springs biasing reaction vessels against the flow restriction device as in Zhou et al. to impose an effective seal yet relieve excess pressure when necessary.

Referring to claim 27, Cody et al. do not disclose a circumferential groove formed in one of the base and cover and a gasket disposed within the groove to provide a seal between the base and cover. Zhou et al. disclose the top seal between reaction block (100) and reaction block cover plate (200) through a single cover plate seal (210) by an O-ring that runs along the perimeters of the cover plate and reaction block (see COL. 14, lines 66 and 67; COL. 15, lines 1-3; FIG. 1). An O-ring groove (240) is provided for the O-ring either in the top surface of the reaction block (100) or bottom surface of cover plate (200) (see COL. 7-12; FIG 8B). Furthermore, a recess (244) may be cut into the underside of cover plate (200). Since the top of the reaction block (100) is slightly

smaller than the recessed area, the reaction block just fits into the area to help position the cover plate on the reaction block (see COL. 12-18; FIG. 8B). Therefore, it would have been obvious to one having ordinary skill in the art to modify the apparatus of Cody et al. include a groove in the base or cover as in Zhou et al. to fit the gasket within it to provide an effective seal and help locate the cover plate on the reaction block.

Referring to claim 28, Cody et al. do not disclose the base and cover each with a periphery flange configured for mating. Zhou et al. disclose a reaction base plate (300) with a recessed area (350) to contain the sliding seal plate (400) and reaction block (100) (see COL. 17, lines 53-61; FIG. 1 and 9). A portion of the reaction base plate (300) extends beyond the sliding seal plate (400) and reaction block (100), where reaction block closure posts (320) receive fasteners through through-holes (230) on the edge of the cover plate (200) to effect a tight seal (see COL. 15, lines 27). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the apparatus of Cody et al. to include periphery flanges as in Zhou et al. to effect a tight seal between the base and cover.

7. Alternatively, claim 51 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,324,483 to Cody et al. as applied to claim 42 above, and further in view of U.S. Patent No. 6,309,608 to Zhou et al.

Referring to claim 51, while the housing of Cody et al. is configured to sustain pressures substantially above atmospheric pressure, Cody et al. do not specifically address the pressure of the fluid for pressurizing the chamber. Zhou et al. disclose a small space or gap located between the top surface of the reaction block (100) and bottom

surface of the cover plate (200) permits fluid communication between the gas and vapor space and reaction chambers (110), facilitating pressure equalization above, below, and within the chambers (see COL. 15, lines 56-67; COL. 16, lines 1-7). Clamping or closure means, typically screw or bolt-type fasteners passing through through-holes, provide an effective seal between the cover plate and reaction block to allow internal reaction block pressures as high as several atmospheres as necessary for particular reactions (see COL. 15, lines 21-32). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use fluid pressurized substantially above atmospheric pressure as necessary to perform synthesis or screening.

8. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,324,483 to Cody et al. as applied to claim 1 above, and further in view of U.S. Patent No. 5,529,756 to Brennan et al.

Referring to claim 8, Cody et al. do not disclose a quick release fitting coupled to the inlet port for connection to a pressure source. Cody et al. do disclose ports (23) on the sidewalls of the cover (20) for introducing or exhausting gas or liquid (see COL. 9, lines 27-34). It is both well known and obvious to provide a fitting for connection to the pressure source as evidenced by Brennan et al. Brennan et al. disclose an inlet tube (72) coupled to the gas inlet (70) for connecting the latter with a gas source to provide a positive pressure within the pressure chamber without introducing oxygen from the environment (see FIG. 5; COL. 46-50). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include an inlet tube as disclosed by Brennan et al. coupled to the gas inlet of the apparatus of Cody et al. to

provide a positive pressure in the chamber without introducing oxygen from the environment.

9. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,324,483 to Cody et al. and U.S. Patent No. 6,309,608 to Zhou et al. as applied to claims 11 and 12 above, and further in view of U.S. Patent No. 6,171,555 to Cargill et al.

Referring to claim 13, Cody et al. in view of Zhou et al. do not quantify the internal volume of the wells. Cargill et al. disclose each reaction chamber having an internal volume of approximately 2 ml. While Cargill et al. do not explicitly state why an internal volume of approximately 2 ml is used for each reaction chamber, Examiner takes Official Notice of the fact that wells with an internal volume of approximately 2 ml is conventional in the art. Furthermore, the internal volume of the well is not a patentable limitation, as the volume can be catered to the amount of sample. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to create wells with an internal volume of approximately 2 ml as disclosed by Cargill et al. due to set standards and as necessary to contain the desired amount of sample.

10. Claims 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,324,483 to Cody et al. as applied to claim 1 above, and further in view of U.S. Patent No. 6,309,608 to Zhou et al., U.S. Patent No. 6,027,694 to Boulton et al., and U.S. Patent No. 6,264,891 to Heynaker et al.

Referring to claim 14, Cody et al. do not explicitly disclose 12 reaction wells arranged in a 3 by 4 array. Zhou et al cite reaction blocks generally have from 12 to 96

or more reaction chambers (see COL. 10, lines 16-18). Boulton et al. disclose microplates with lower density wells are available as needed for the number of assays performed (see COL. 1, lines 53-57). While Boulton et al. and Zhou et al. do not mention the configuration of the wells, Heynaker et al. leave the option of array configuration of wells open (see COL. 6, lines 57-63). Heynaker et al. do not explicitly state why different arrays are used; however, it appears that configuration may be important for automation. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use 12 wells for completing lesser than or equal to 12 reactions in a 3 by 4 array to conform to automation equipment.

Referring to claim 15, Cody et al. in view of Zhou et al., Boulton et al., and Heynaker et al. do not quantify the internal volume of the wells. Applying the decision made by the Federal Circuit in Gardner v. TEC Systems, Inc., the dimensions of the well would not affect the performance of the claimed device respective to prior art device. It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the internal volume of the wells as necessary to produce the desired amount of product. Therefore, the claimed device is not patentably distinct from prior art device based on the internal volume of the wells.

11. Claims 20, 36, and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,324,483 to Cody et al. as applied to claims 1, 17, 31, 33, and 42 above, and further in view of U.S. Patent No. 5,443,791 to Cathcart et al.

Referring to claims 20, 36, and 48, while the flow restriction device of Cody et al. permits and restricts flow into the wells, Cody et al. do not explicitly state check valves

aligned with reaction wells to permit and restrict flow into wells. Cathcart et al. disclose a duck-billed closure (253) assembled to a tube (255) located in the storage stations of the automated laboratory (11) (see ABSTRACT; FIGS 7A-C; COL. 18, lines 60 and 61). A needle-like device may be inserted or withdrawn from above to allow or restrict flow into the tube, respectively. Furthermore, the duck-bill closure minimizes evaporation and prevents contamination (see COL. 19, lines 39-44; ABSTRACT). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to have check valves aligned with the wells to allow or restrict flow into the wells and restrict flow from the wells into the pressure chamber while minimizing evaporation and preventing contamination.

12. Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,324,483 to Cody et al.

Referring to claim 30, Cody et al. do not quantify the volume of the pressure chamber. The Federal Circuit decided in Gardener v. TEC System, Inc. that difference of dimensions between prior art and claims would not make the claimed device perform differently than prior art device, and the claimed device is not patentably distinct from the prior art device. Furthermore, the applicant has not stated how a pressure chamber volume of 10 cubic inches solves any problems or is for any particular purpose. It appears that the synthesis apparatus would perform equally well with any pressure chamber volume. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use different pressure chamber volumes as necessary or desired for performing assays.

13. Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,324,483 to Cody et al. as applied to claim 31 above, and further in view of U.S. Patent No. 4,180,943 to Smith et al. and U.S. Patent No. 6,250,707 to Dinter et al.

Referring to claim 32, Cody et al. do not disclose a four bar mechanism for fastening the cover onto the reaction block. Smith et al disclose a four bar mechanism for an aircraft door, which forces the latch operation to be performed in correct order (see COL. 1, lines 29-38). Additionally, Dinter et al. disclose further advantages of simple, reliable mechanism with low production cost, high precision, and good functionality (see COL. 1, lines 51 and 52; COL. 2, lines 4-6). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use a four bar mechanism as in Smith et al. and Dinter et al. for fastening a cover onto the reaction block for the apparatus of Cody et al. for advantages of simple, reliable mechanism with low production cost, high precision, and good functionality.

Response to Arguments

1. Applicant's arguments filed 10/18/2002 have been fully considered but they are not persuasive.

2. Applicants submit that Cody et al. do not anticipate the apparatus as set forth in claim 1.

3. Cody et al. disclose all the structural limitations in claim 1. Referring to FIG. 5, the apparatus has a base (15), cover (20), and inlet port (23). The base (15) has a plurality of reaction wells (16) formed in the upper surface of the base (15), as evident by the aperture through the upper surface of the base (15). Each reaction well (16) extends partially through the lower portion (41) of the base (15), as evident by recesses extending two-thirds through the

lower portion (41) or the base (15), yielding reaction wells (16) with closed lower ends as defined by the lower portion (41) of the base (15). Each of the reaction wells (16) has an open upper end, as evident by the aperture in the upper portion of the base and reaction tubes (11) passing through the aperture in the upper portion of the base and residing in the recesses extending two-thirds through the lower portion (41) of the base (15). These reaction tubes (11) receive the components for the reaction. A cover (20) is configured for sealing engagement with the base (15) to form an airtight housing enclosing the plurality of reaction wells (16) (see COL. 9, lines 25-27). According to Merriam-Webster's Collegiate Dictionary, engage is to cause (mechanical parts) to mesh, which is to fit or work together properly, or to come together and interlock, which is to lock together, unite, or connect so that the motion or operation of any part is constrained by another (as of machinery parts), or be or become in gear. The cover (20) meshes, comes together, interlocks, locks together, unites, or connects the cover (20) with the base (15) such that the parts fit or work together properly or such that the parts connect so that the motion or operation of the base is constrained by the cover, and vice versa. The housing formed by the union of the cover (20) and base (15) defines a common pressure chamber in communication with the plurality of reaction wells (16), as evident by the reaction tubes (11) smaller than the apertures in the first (24) and second (26) gaskets leading into the reaction wells (16) (see COL. 8, lines 58-68; COL. 9, lines 1-67; COL. 10, lines 1-7). An inlet port (23) is in communication with the pressure chamber for supplying pressurized fluid to the chamber to pressurize the plurality of reaction wells (16), as Cody et al. disclose that ports (23) can be adapted to perform as inlet ports so that gaseous and/or liquid materials may be introduced into

the manifold and allow control over the atmosphere within the manifold, such as pressurization, or sparging of the reaction tubes (11) (see COL. 9, lines 25-36 and 46-50).

4. Applicants submit that the Cody et al. patent is directed to solid phase synthesis, which focuses on chemical reactions of substrates attached to solid supports, including methods for attachment and detachment from the supports. Applicants further submit that there is no teaching in Cody et al. that covers pressurization substantially above atmospheric pressure since solid phase synthesis applications of small organic molecules typically do not use a pressurized reacting gas. Applicants further submit that the apparatus is pressurized in the context of manipulation (i.e. forcing liquid contents of reaction wells through a filter plate) not reaction. Applicants further submit such manipulation requires only nominal pressure or inert atmosphere. Applicants further submit Cody et al. do not disclose an apparatus configured for pressurization substantially above atmospheric pressure.

Whether or not the apparatus is used for solid phase synthesis or the pressurized fluid is used for forcing liquid contents of reaction wells through a filter or reaction, Examiner emphasizes that the claims are apparatus claims and the manner of operation is considered to be merely a statement of intended use. They do not add structure to the claimed apparatus. The fluid is pressurized, and since the internal environment of the housing is initially atmospheric pressure as pressure not vacuum is being applied, the internal environment of the housing is above atmospheric pressure. According to Merriam-Webster's Collegiate Dictionary, pressurize is to confine the contents of under a pressure greater than that of the outside atmosphere; to apply pressure to; or to design to withstand pressure.

The housing is configured to sustain a pressure substantially above atmospheric. Applicants disclose on page 12, lines 6-11: The reactor vessel is preferably designed to withstand pressures substantially above atmospheric pressure (i.e. 14.7 psi). The vessel is preferably designed to withstand pressures above 10 psig, and more preferably pressures above 50 psig. The vessel may also be designed, for example, to operate at pressures 15 psig, 20 psig, 30 psig, 40 psig, 100 psig, 300 psig, 500 psig, 1000 psig, or other selected pressures. Applicant does not specify what constitutes "substantially" in the specification. If "substantially" is the ability to withstand pressures above 10 psig as it is listed as a preferred pressure in the specification, the pressure is considered "nominal" or "inert" pressure since 10 psig is less than 1 atmosphere. However, the specification does not exclude "substantially" from pressures of just above 1 atmosphere or 14.7 psi, such as 1.01 atmosphere or 14.84 psi. Claim 1 is broad and does not specify what pressure the housing is configured to withstand. Is it the differential pressure, external pressure, or internal pressure? According to Merriam-Webster's Collegiate Dictionary, to configure is to set up for operation especially in a particular way. The housing is "configured" or "set up" such that it could withstand a pressure above atmospheric pressure. It does not necessarily have to since "configured" does not positively recite. Furthermore, the housing is set up to withstand a pressure above atmospheric pressure, as the housing needs to be able to withstand a pressure above atmospheric pressure or else the assembly including the housing would not sustain itself and just topple from the external atmospheric pressure acting upon it. Cody et al. disclose the apparatus allowing manipulations, such as pressurization (see COL. 9, lines 46-50). The use of pressurized gas is necessary in the process of promoting and completing the reaction of reactants embedded in the solid supports with injected reactants by providing a

controlled environment and draining or expelling excess reagents, solvents, and by-products (see COLS. 13-14). In fact, injecting reactants into the reaction tubes requires an initial thrust of air pressure to force the reactants into the reaction tubes.

Cody et al. disclose that the apparatus is made of materials that are capable of withstanding pressures required for organic synthesis. The reaction tubes can be made of glass, polytetrafluoroethylene (PTFE), stainless steel, ceramics, or alternate glasses, metals, or plastics, preferably glass (see COL. 8, lines 3-10). In a preferred embodiment, the reaction wells are made of a transparent material, such as glass, plexiglass, or alternate glasses, or plastics, such that reactions may be visually monitored (see COL. 8, lines 52-57). The reservoir rack is made of materials, including glass, stainless steel, PTFE, ceramics, and various types of plastics, metals, or glasses, preferably glasses (see COL. 8, lines 29-38). The holder block is preferably constructed from a heat-resistant material, such as PTFE, stainless steel, ceramics, glass, or certain types of metals, glasses, or plastics, such that it will be able to withstand organic reaction conditions (see COL. 9, lines 11-15). In a preferred embodiment, the manifold is made of a transparent material, such as glass, plexiglass, or alternate glasses or plastics, such that reactions may be visually monitored (see COL. 9, lines 36-41). The capability to withstand pressures substantially above atmospheric pressure is inherent to metals, such as stainless steel. In fact, Applicant's specification on page 11, lines 15 and 16 disclose that the base and cover may be made from steel, a material allowing the apparatus to operate at high pressure (10-1000 psig). The thickness of the materials plays a significant role in the ability of a material to withstand pressure. Increasing the thickness of any material would increase its ability to withstand greater pressures.

5. Applicant submits that Cody et al. do not show a flow restriction device positioned adjacent to open ends of the reaction wells to provide communication between the reaction wells and pressure chamber while reducing cross-talk between the reaction wells. Applicant further submits that the gasket (26) of Cody et al. does not provide communication between the reaction wells and sealed chamber (i.e. chamber formed by manifold 20). Applicant further submits that the gaskets (24,26) are used to seal the reaction wells from the chamber as described in COL. 9, lines 46 and 47, and gasket (26) seals the open ends of the reaction wells (16) from one another. Applicant further submits that there are no vent holes or micromachined flow restrictions formed in the gasket.

> Referring to FIG. 5, the flow restriction device (26) is positioned adjacent to the open ends of the reaction wells, as evident by the aperture in the gasket closely surrounding the reaction tube (11) inserted through the aperture into the reaction well (16) via the open end of the reaction well. The flow restriction device (26) provides communication between the reaction wells and pressure chamber, as evident by the flow restriction device (26) closely surrounding the reaction tube (11) with a slight gap between the flow restriction device (26) and reaction tube (11) such that pressurized gas may travel from the pressure chamber into the reaction well. Communication between the flow restriction device (26) and pressure chamber is also demonstrated by pressurized gas traveling from the pressure chamber through the reaction tube within the flow restriction device (26) and out of the filter and into the reaction well (16). The flow restriction device (26) prevents cross-talk among reaction wells as the flow restriction device (26) covers the reservoir block (15) with reaction wells, and the apertures in the

flow restriction device (26) are aligned with the reaction wells (16), which received reaction tubes (11), such that contents of a reaction well or tube is sufficiently prevented from flowing into another reaction well or tube.

In COL. 9, lines 46 and 47, Cody et al. disclose "Such placement of a first gasket(s) creates a sealing effect between the manifold and the holder block in order to allow manipulations, such as pressurization, inert atmosphere, and **chilled gas circulation** to take place." The gaskets (24,26) do not seal the reaction wells from the chamber. The gaskets (24,26) provide an effective seal among the layers of cover (20), holder block (18), and base portion (15,41), such that an airtight internal environment can be provided to maintain a pressurized environment. If the gaskets sealed the reaction wells from the chamber, gas circulation cannot take place within the apparatus. Furthermore, access to the reaction wells from the pressure chamber is provided through the reaction tube in which the lower or filter portion contacts the reaction well. The gaskets do not seal the open ends of the reaction wells from one another. Actually, an aperture in the gasket is provided for alignment with the open end of the well. A reaction tube just takes up most of the space of the aperture in the gasket. Cody et al. disclose several times that it is not necessary to fully utilize the apparatus of the present invention. Therefore, the reaction tubes might not be used. Whether the gaskets seal the reaction wells from the chamber or provide an effective seal among the layers to provide an airtight environment for pressurization, Examiner emphasizes the claims are directed toward an apparatus, and the manner of operation is considered to be merely a statement of intended use. They do not add structure to the claim.

The apertures in the gaskets (24,26) are vent holes or micromachined flow restrictions. Whether venting occurs through the reaction tube situated in the aperture and/or slight gap from the gasket closely surrounding the reaction tube (11) and/or aperture without the reaction tube since Cody et al. disclose that it is not necessary to fully utilize the apparatus of the present invention, it is inevitable that some gas will be vented through the aperture from the reaction well during the process of pressurization. Whether the vent holes are micromachined or drilled, Examiner emphasizes that in a product-by-process claim patentability is based on the product and does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious over a product of the prior art, the claim is unpatentable even though the prior art product was made by a different process. Therefore, since Cody et al. provide the teaching for vent holes, Cody et al. anticipate the claims of micromachined flow restrictions since the manner in which the flow restrictions or vent holes are made is not given patentable weight.

6. Applicant submits that the apparatus as set forth in claim 31 is not anticipated by Cody et al., which do not show a pressure chamber sized for receiving a microtiter plate. The chamber of Cody et al. is formed by manifold 20 and holder block 18 and is configured for receiving reaction tubes 11 (Fig. 4).

The pressure chamber is "sized" for receiving a microtiter plate. According to Merriam-Webster's Collegiate Dictionary, "sized" is to make a particular size or bring to proper or suitable size. The pressure chamber is "sized" such that any microtiter plate can be received within its chamber. The pressure chamber does not necessarily have to

receive the microtiter plate as presented in Cody et al. The claim does not specify that the pressure chamber receive the microtiter plate. In Cody et al. the pressure chamber is provided by the manifold (20) with an opening for receiving a microtiter plate, and the opening is "sized" for receiving a microtiter plate in different orientations. Since microtiter plates are commercially available in a variety of sizes, the pressure chamber of Cody et al. is surely "sized" for receiving any of those microtiter plates.

7. Referring to claims 2-4, 52, and 53, Applicant submits that the apparatus of Cody et al. is not designed to operate at pressure substantially above atmospheric pressure and does not disclose sustaining pressures above 40 psig. Applicant further submits that the apparatus of Painter et al. does not include individual reaction wells for parallel synthesis or screening and is not concerned with sealing individual reaction wells. Applicant further submits that Cody et al. is generally limited to solid phase synthesis (see COL. 3, lines 1-3), whereas Painter et al. deal with gas phase polymerization. Applicant further submits the apparatus of Cody et al. is designed to operate at low pressures (e.g. nominal pressure for physical manipulations or inert atmosphere) and would require significant modification for operation substantially above atmospheric pressure not just with regard to the manifold material but also as to the sealing arrangement and simple spring clips to hold the assembly together.

Cody et al. disclose an apparatus for operating at pressures substantially above atmospheric pressure as discussed above. Cody et al. does not disclose sustaining pressures above 40 psig. Painter et al. disclose a Plexiglas reactor for withstanding 10 psi to 1000 psi to carry out operations requiring elevated pressures and/or handling reactive materials at elevated pressures. Both the apparatus of Cody et al. and Painter et al. deal

with synthesis whether it is solid phase synthesis or gas phase polymerization. Painter et al. address the need for an apparatus dealing with certain pressures necessary for certain syntheses. Painter et al. provide the motivation for an apparatus withstanding certain pressures as required by certain syntheses. It does not matter whether Painter et al. include individual reaction wells for synthesis or is concerned with sealing the individual reaction wells, as Cody et al. provide these limitations. The secondary reference Painter et al. does not have to provide all the limitations in the claims. Painter et al. serve to provide motivation for the limitation not explicitly taught by Cody et al. The apparatus of Cody et al. would not require significant modification for operation substantially above atmospheric pressure. In Cody et al. the pressure chamber can be made from a variety of materials, one of them being plexiglass. The reactor of Painter et al. is not only made of plexiglass but also withstands pressures from 10-1000 psi. This provides evidence that the apparatus of Cody et al. can provide pressure substantially above atmospheric pressure, 10-1000 psi. Since Cody et al. provide the limitation of the sealing arrangement as recited in the claims or the base claims from which they depend, it would appear that the sealing arrangement can withstand the pressures substantially above atmospheric pressure otherwise the sealing arrangement in the immediate application could not withstand pressures substantially above atmospheric pressure. Furthermore, the limitation in the claim is the pressure chamber configured to withstand pressures above atmospheric pressure not the sealing arrangement configured to withstand pressures above atmospheric pressure. The fastening mechanisms have not been recited in the claims or the base claims from which they depend, and therefore, should not be

considered in their contribution to withstanding pressures above atmospheric pressure. Furthermore, the limitation in the claim is the pressure chamber configured to withstand pressures above atmospheric pressure not the fastening mechanisms configured to withstand pressures above atmospheric pressure.

8. Referring to claims 2-4, 52, and 53, Applicant submits that Heiszwolf discusses stability criteria for batch and continuous reactors. Applicant further submits that the reactor is enclosed by a Plexiglass box to prevent injury to lab personnel in the case of a reactor explosion. Applicant further submits that the plexiglass box is not used to create a pressure chamber suitable for sustaining pressure during a reaction. Applicant further submits that the Grunwald et al. reference is directed to coolant mixing in pressurized water reactors and does not remedy the deficiencies of the primary reference.

Heiszwolf provides more support that a transparent plexiglass reactor is able to withstand pressures substantially above atmospheric pressure. Heiszwolf also provides motivation for providing a transparent plexiglass reactor capable of withstanding pressures substantially above atmospheric pressure to prevent dangers to personnel working with the apparatus. Technically, the plexiglass box could be a pressure chamber for sustaining pressure during a reaction.

Applicant does not explain why Grunwald et al. do not remedy the deficiencies of the primary reference. Cody et al. disclose an apparatus for operating at pressures substantially above atmospheric pressure as discussed above. Grunwald et al. disclose a transparent plexiglas reactor for withstanding substantially high pressures to carry out operations requiring elevated pressures and/or handling reactive materials at elevated

pressures. Both the apparatus of Cody et al. and Grunwald et al. deal with synthesis. Grunwald et al. address the need for an apparatus dealing with certain pressures necessary for certain syntheses. Grunwald et al. provide the motivation for an apparatus withstanding certain pressures as required by certain syntheses. It does not matter whether Grunwald et al. include individual reaction wells for synthesis or is concerned with sealing the individual reaction wells, as Cody et al. provide these limitations. Grunwald et al. serve to provide motivation for the limitation not explicitly taught by Cody et al. The apparatus of Cody et al. would not require significant modification for operation substantially above atmospheric pressure. In Cody et al. the pressure chamber can be made from a variety of materials, one of them being plexiglass. The reactor of Grunwald et al. is not only made of transparent plexiglass but also withstands high pressures.

Cody et al. provide the structural limitations of the base claims except for pressure. Painter et al. provides the teaching of pressures 10-1000 psi using the material of plexiglass as cited in Cody et al. for the pressure chamber. Heiswolf and Grunwald et al. provide the motivation for using transparent plexiglass for monitoring reactions and their ability to withstand high pressures.

9. Referring to claim 5, Applicant submits that the Examiner cited Ischikawa et al. for its use of a titanium pressure vessel. Applicant further submits that as previously discussed, the apparatus of Cody et al. is designed to operate at very low pressures and would require significant modification for operation substantially above atmospheric pressure, not just with regard to the material of the manifold.

The apparatus of Cody et al. would not require significant modification for operation substantially above atmospheric pressure. In Cody et al. the pressure chamber can be made from a variety of materials, one of them being plexiglass. The reactor of Painter et al. is not only made of plexiglass but also withstands pressures from 10-1000 psi. This provides evidence that the apparatus of Cody et al. can provide pressure substantially above atmospheric pressure, 10-1000 psi. Since Cody et al. provide the limitation of the sealing arrangement as recited in the claims or the base claims from which they depend, it would appear that the sealing arrangement can withstand the pressures substantially above atmospheric pressure otherwise the sealing arrangement in the immediate application could not withstand pressures substantially above atmospheric pressure. Furthermore, the limitation in the claim is the pressure chamber configured to withstand pressures above atmospheric pressure not the sealing arrangement configured to withstand pressures above atmospheric pressure. The fastening mechanisms have not been recited in the claims or the base claims from which they depend, and therefore, should not be considered in their contribution to withstanding pressures above atmospheric pressure. Furthermore, the limitation in the claim is the pressure chamber configured to withstand pressures above atmospheric pressure not the fastening mechanisms configured to withstand pressures above atmospheric pressure.

Ischikawa et al. disclose a titanium pressure vessel, which can withstand high pressures and resist corrosion. Therefore, it would be advantageous to modify the apparatus of Cody et al. to make it from titanium as in Ischikawa et al. for withstanding high pressures and resisting corrosion.

10. Referring to claims 6, 7, 9, 11, 12, 16, 26, 27, 50, and 51, Applicant submits that Zhou et al. do not remedy the deficiencies found in the primary reference, as previously discussed. Applicant further submits that Zhou et al. do not show or suggest a flow restriction device, and thus, flow between the reaction vessels is not restricted by the septum sheet. Applicant further submit that the springs (490) of the Zhou et al. apparatus are used to force seal plate (400) towards the bottom surface of reaction block (100) and not for biasing vials. Applicant further submits that glass vials are not used in the reaction block (100) because vials would make it impossible to open the reaction wells and drain or purge the contents, which is an important feature of the Zhou et al. apparatus.

While cover plate seal (210) may be considered the flow restriction device, it is not required for Zhou et al. to disclose a flow restriction device. Zhou et al. serve to provide motivation for the limitations not explicitly disclosed in Cody et al. The primary reference Cody et al. already discloses the flow restriction device. Whether or not the springs are for biasing the vials upward against the flow restriction device, Examiner emphasizes that the manner of operating the device does not differentiate the apparatus claims from the prior art. MPEP 2114. A recitation with respect to the manner in which a claimed apparatus is intended to be employed does not differentiate the claimed apparatus from a prior art apparatus if the prior art apparatus teaches all the structural limitations of the claim. Therefore, since Zhou et al. disclose the springs at the bottom of the reaction wells, Zhou et al. meet the limitation in claim 26. Furthermore, the springs are biasing the vials upward, as the vials would be in a lower position without the springs. The springs bias the vials upward, and when the pressure within the apparatus becomes

excessive, the springs compress to relieve such pressure. "Upward" is a relative term and has not been defined.

11. Applicant submits that the additional references cited U.S. Patent Nos. 5,529,756 to Brennan et al., 6,171,555 to Cargill et al., 6,027,694 to Boulton et al., 6,264,891 to Heynaker et al., 5,443,791 to Cathcart et al., 4,180,943 to Smith et al., and 6,250,707 to Dinter et al. do not remedy the deficiencies of the primary references.

Applicant has not explained why the references do not remedy the deficiencies of the primary references. The primary references provide the most of the structural limitations, and the references cited provide motivation for providing the limitation not explicitly taught by the primary references.

Conclusion

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. WO 01/05497 to Flanagan et al. anticipates at least claim 1. However, there is not 102(e) date since US has not been designated and the filing date was not on or after 11/29/2000.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Quan whose telephone number is (703) 305-1947. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (703) 308-4037. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 879-9310 for regular communications and (703) 872-9311 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

Elizabeth Quan
Examiner
Art Unit 1743

eq
December 23, 2002

Arlen Soderquist

ARLEN SODERQUIST
PRIMARY EXAMINER